REMARKS

Applicant has amended claims 1, 2, 5, 6, 43, 49-54 and 56-59, and have canceled claims 3, 4, 7-42, 44, 47, 48 and 55-60, during prosecution of this patent application. Applicants are not conceding in this patent application that said amended and canceled claims are not patentable over the art cited by the Examiner, since the claim amendments and cancellations are only for facilitating expeditious prosecution of this patent application. Applicant respectfully reserves the right to pursue said amended and canceled claims, and other claims, in one or more continuations and/or divisional patent applications.

In the amended claim 1, the feature of "wherein said oxidized heparin fraction being super-sulfated is characterized by said oxidized heparin fraction being O-sulfated at vertexes of repeating units of the oxidized heparin fraction" is supported in the specification, Paragraphs 52-53 on pages 18-19 and is illustrated in Figure 1.

In the amended claim 1, the feature of "wherein said oxidized heparin fraction comprises a sulfate to carboxylate ratio sufficiently high to fully inhibit angiogenesis" is supported in Table 3 on page 29. Table 3 shows that the FGF2 + oxidized ultra-LMWH reduces the FGF2-stimulated cell tube formation from 79.83 to 47.54 which is about 15% higher than the control (PBS) of 41.36, so that the FGF2 + oxidized ultra-LMWH partially, but not fully, inhibits angiogenesis. In contrast, Table 3 shows that the FGF2 + super-sulphated oxidized ultra-LMWH reduces the FGF2-stimulated cell tube formation from 79.83 to 40.20 which is at the level of the control (PBS) of 41.36, so that the FGF2 + super-sulphated oxidized ultra-LMWH fully inhibits angiogenesis.

The features specific to new claims 91 and 92 are supported in the specification, Paragraph 29 on page 9.

The Examiner rejected claims 1, 2, 5, 6, 43, 49-54, 56-59 and 61-63 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Mascellani *et al.* (Mascellani (U.S. Patent 4,973,580) in combination with Weitz *et al.* (Weitz) (U.S. Patent 6,075,013) in view of Cohen *et al* . (Cohen) (U.S. Patent 5,908,837) in combination with Scholander (U.S. Patent 4,461,665).

Applicant respectfully traverses the § 103 rejections with the following arguments.

35 U.S.C. § 103(a)

The Examiner rejected claims 1, 2, 5, 6, 43, 49-54, 56-59 and 61-63 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Mascellani *et al.* (Mascellani (U.S. Patent 4,973,580) in combination with Weitz *et al.* (Weitz) (U.S. Patent 6,075,013) in view of Cohen *et al* . (Cohen) (U.S. Patent 5,908,837) in combination with Scholander (U.S. Patent 4,461,665).

Applicant respectfully contends that claim 1 is not unpatentable over Mascellani in combination with Weitz in view of Cohen in combination with Scholander, because Mascellani in combination with Weitz in view of Cohen in combination with Scholander does not teach or suggest each and every feature of claim 1.

As an example of why claim 1 is not unpatentable over Mascellani in combination with Weitz in view of Cohen in combination with Scholander, Mascellani in combination with Weitz in view of Cohen in combination with Scholander does not teach or suggest the feature: "wherein the super-sulfated oxidized heparin fraction has a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction; wherein the super-sulfated oxidized heparin fraction comprises a sulfate to carboxylate ratio sufficiently high to fully inhibit angiogenesis".

For clarification purposes, Applicant notes that claim 1 is not claiming a process of forming the super-sulfated oxidized heparin fraction by performing sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction. Rather, claim 1 is claiming a chemical structure that results from performing sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction. Note that new claim 94 is claiming this process.

The Examiner argues: "Mascellani discloses that the oxidation process does not change the sulfate content of heparin ... With regard to an oxidized heparin fraction, which is super-sulfatedof claim 1, it would be within the scope of the artisan in this art to isolate a heparin fraction which is rich in sulfate groups through routine chromatography experimentationas taught by Weitz, because sulfated heparin are well known for their thrombolytic activities."

In response, Applicants note that Mascellani, col. 4, lines 36-40 teaches away from the claimed super-sulfation by asserting that the sulfate to carboxylate ratio in the depolymerized product is the same as sulfate to carboxylate ratio in the starting product (heparin).

In further response, Applicants assert that Weitz does not disclose a super-sulfated oxidized heparin fraction hasving "a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction" as required by claim 1.

Furthermore, the feature of the super-sulfated oxidized heparin fraction having "a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution at oxygen bonds at vertexes of repeating units of the first oxidized heparin fraction" requires that the amount of sulfation present in the super-sulfated oxidized heparin fraction exceed the amount of sulfation present in the first oxidized heparin fraction. However, Weitz does not disclose that the amount of sulfation in the heparin fractions observed through routine chromatography experimentation exceeds the amount of sulfation in the heparin from which the heparin fraction are derived.

In addition, Mascellani in combination with Weitz in view of Cohen in combination with Scholander does not disclose "wherein the super-sulfated oxidized heparin fraction comprises a sulfate to carboxylate ratio sufficiently high to fully inhibit angiogenesis". None of the

preceding references cited by the Examiner disclose the effect of O-sulfation of oxidized heparin fractions on angiogenesis. None of the preceding references cited by the Examiner disclose that angiogenesis could be fully inhibited by sufficient O-sulfation of oxidized heparin fractions. The specification of the present patent application not only discloses experimental results demonstrating that sufficient O-sulfation of oxidized heparin fractions totally inhibits angiogenesis (as discussed *supra* in conjunction with Table 3 on page 29 of Applicant's specification), which is an unknown and unexpected result, but also enables the employment of O-sulfation in Paragraphs 52 and 53 of Applicant's specification for implementing the super-sulfation of the present invention and such enablement is unknown in the prior art.

Moreover, it would not be obvious to super sulfate the oxidized heparin fraction as claimed by Applicant, because the present invention's use of said super sulfation to fully inhibit angiogenesis is an unexpected result, as evidenced by Lars Lundin et al., Selectively Desulfated Heparin Inhibits Fibroblast Growth Factor-induced Mitogenicity and Angiogenesis, Journal of Biological Chemistry, Vol. 275, No. 32 (August 11, 2000), (hereinafter, "Lundin") included herewith in Appendix A. Lundin teaches that ***desulfation of heparin*** inhibits angiogenesis. For example, see Lundin's Abstract ("FGF-2 induced angiogenesis in chick embryos was inhibited by 6-O-desulfated heparein"). In contrast, Applicant is claiming sulfation of an oxygenated heparin fraction to inhibit angiogenesis, which is the exact opposite of desulfation. In light of Lundin's teaching of desulfation for inhibiting angiogenesis, Applicant's teaching that sulfation of an oxygenated heparin fraction (in the manner described in Applicant's specification and claimed in claim 1) totally inhibits angiogenesis is an ***unexpected result***. Therefore, it would not be obvious to a person of ordinary skill in the art at the time of conception of Applicant's invention to super sulfate the oxidized heparin fraction as claimed by Applicant in claim 1.

Therefore, Mascellani in combination with Weitz in view of Cohen in combination with Scholander does not disclose the preceding feature of claim 1.

Based on the preceding arguments, Applicant respectfully maintains that claim 1 is not unpatentable over Mascellani in combination with Weitz in view of Cohen in combination with Scholander, and that claim 1 is in condition for allowance. Since claims 2, 5, 6, 43, 49-54, 56-59 and 61-63 depend from claim 1, Applicant contends that claims 2, 5, 6, 43, 49-54, 56-59 and 61-63 are likewise in condition for allowance.

In addition, Applicants point out that the features specific to claim 93 were in claim 1 prior to being deleted from claim 1 by amendment herein. In the present office action, the Examiner alleged that said features specific to claim 93 (previously in claim 1) recite an intended use.

In response, Applicants respectfully contend that said features specific to claim 93 do not recite an intended use, but rather recite properties possessed by the oxidized heparin fraction. There is no language in said features specific to claim 93 that express an intended use.

Said features specific to claim 93 are analogous to "a material that is sufficiently brittle as to fracture upon being subjected to a cooling rate of at least 10 degrees F per second". The preceding material possesses the recited feature of brittleness even if the material is not subjected to the cooling rate of at least 10 degrees F per second. Similarly, the properties of the oxidized heparin fraction expressed in said features specific to claim 93 exist even if the oxidized heparin fraction is not present in human blood.

Therefore, Applicants respectfully request that the Examiner examine the features specific to claim 93 as having patentable significance as properties of the oxidized heparin fraction.

CONCLUSION

Based on the preceding arguments, Applicant respectfully believes that all pending claims and the entire application meet the acceptance criteria for allowance and therefore request favorable action. If the Examiner believes that anything further would be helpful to place the application in better condition for allowance, Applicant invites the Examiner to contact Applicant's representative at the telephone number listed below. The Director is hereby authorized to charge and/or credit Deposit Account 19-0513.

Date: 12/31/2007

Jack P. Friedman
Registration No. 44,688

Schmeiser, Olsen & Watts
22 Century Hill Drive - Suite 302
Latham, New York 12110
(518) 220-1850